

84. (Amended) A method of obtaining a member of a specific binding pair, the method comprising:

contacting a library of filamentous bacteriophage particles [according to claim 76] with a desired ligand,

wherein said filamentous bacteriophage particles display on their surface as a fusion with a coat protein surface component a polypeptide which is a specific binding pair member with ability to bind a complementary ligand, the particles containing nucleic acid encoding said fusion, said nucleic acid including a sequence encoding said polypeptide provided by mutation of nucleic acid encoding a specific binding pair member comprising an enzyme or fragment thereof, which enzyme or fragment thereof is able to bind a ligand and is at least 200 amino acids,

wherein said filamentous bacteriophage particles display a population of specific binding pair members, and

separating particles displaying specific binding pair members which have a desired enzymatic activity.

REMARKS

In support of the restriction requirement, the Office Action merely states that the inventions of group 1 and 5, 6 are unrelated. The Action states without support that the different inventions of group 1, group 5 and group 6 are drawn to methods of obtaining specific binding pair members using different method steps. That assertion is unfounded as claim groups 1, 5, and 6 are all drawn to methods for producing and selecting members of specific binding pairs and although there are minor differences in the method steps of all three claim groups, the methods are closely related. In fact, claim groups 1, 5 and 6 are all classified in class 435, subclass 69.1.

According to M.P.E.P. §808.02, in order to establish reasons for insisting on restriction, the Examiner must show by appropriate explanation:

- (a) separate classification;
- (b) a separate status in the art when claim groups are classified together; or
- (c) a different field of search.

In the present case, claim groups 1, 5 and 6 are all classified in class 435, subclass 69.1. Further, the Examiner has not shown that the subject matter of claim groups

1, 5 and 6 have achieved a separate status in the art nor that claim groups 1, 5 and 6 would not require a separate field of search.

On that basis, the Applicants submit that claim groups 1, 5 and 6 should be examined together. Applicants therefore, respectfully traverse the restriction requirement as applied to claim groups 1, 5 and 6 and request that these groups be examined simultaneously.

Respectfully submitted,

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28111/32106B

**CLAIMS PENDING AFTER ENTRY OF
AMENDMENT DATED JANUARY 21, 2000**

44. A method of obtaining a specific binding pair member, which method comprises:
- expressing in recombinant host cells a library of nucleic acid sequences encoding a genetically diverse population of polypeptides provided by mutating nucleic acid encoding a specific binding pair member which comprises an enzyme or fragment thereof, which enzyme or fragment thereof is able to bind a ligand and is at least 100-200 amino acids, wherein polypeptides encoded within the library are each expressed as a fusion with a coat protein surface component of a filamentous bacteriophage which displays said polypeptides at the surface of bacteriophage particles, there being packaged in each particle a nucleotide sequence encoding a said fusion, whereby the genetic material of each said particle displaying a polypeptide includes a nucleic acid sequence encoding the polypeptide displayed on that particle.
45. A method according to claim 44 wherein said domain or fragment is at least 200 amino acids.
46. A method according to claim 44 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.
47. A method according to claim 45 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.
48. A method according to claim 44 wherein particles formed by said expression are selected or screened to provide an individual displayed polypeptide specific binding pair member or a mixed population of displayed polypeptide specific binding pair members associated in respective particles with nucleic acid encoding said displayed polypeptide specific binding pair member or members, the specific binding pair member or members thus provided having ability to bind a complementary ligand.
49. A method according to claim 48 wherein the particles are selected by affinity with a complementary ligand.
50. A method according to claim 49 which comprises recovering any particles bound to said complementary ligand by washing with an eluant.
51. A method according to claim 50 wherein the eluant contains a molecule which competes with said particles for binding to said complementary ligand.

28111/32106B

**CLAIMS PENDING AFTER ENTRY OF
AMENDMENT DATED JANUARY 21, 2000**

52. A method according to claim 49 wherein the particles are applied to said complementary ligand in the presence of a molecule which competes with said particles for binding to said complementary ligand.

53. A method according to claim 48 wherein the particles are selected by enzymatic activity.

54. A method of producing a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 48; and
- (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

55. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 48; and
- (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

56. A method of producing a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 49; and
- (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

57. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 49; and
- (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

58. A method of producing a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 53; and
- (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

28111/32106B

**CLAIMS PENDING AFTER ENTRY OF
AMENDMENT DATED JANUARY 21, 2000**

59. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 53; and
- (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

60. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 48, said nucleic acid encoding a polypeptide specific binding pair member or a polypeptide chain component thereof; and

- (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to a polypeptide specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

61. A method of producing a specific binding pair member, the method comprising:

producing by expression from encoding nucleic acid obtained by a method according to claim 60 a said derivative specific binding pair member.

62. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 49, said nucleic acid encoding a polypeptide specific binding pair member or a polypeptide chain component thereof; and

- (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to a polypeptide specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

63. A method of producing a specific binding pair member, the method comprising:

producing by expression from encoding nucleic acid obtained by a method according to claim 62 a said derivative specific binding pair member.

28111/32106B

**CLAIMS PENDING AFTER ENTRY OF
AMENDMENT DATED JANUARY 21, 2000**

64. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 53, said nucleic acid encoding a polypeptide specific binding pair member or a polypeptide chain component thereof; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to a polypeptide specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

65. A method of producing a specific binding pair member, the method comprising:

producing by expression from encoding nucleic acid obtained by a method according to claim 64 a said derivative specific binding pair member.

78. (Amended) A method of obtaining a member of a specific binding pair, the method comprising:

contacting a library of filamentous bacteriophage particles with a desired ligand,

wherein said filamentous bacteriophage particles display on their surface as a fusion with a coat protein surface component a polypeptide which is a specific binding pair member with ability to bind a complementary ligand, the particles containing nucleic acid encoding said fusion, said nucleic acid including a sequence encoding said polypeptide provided by mutation of nucleic acid encoding a specific binding pair member comprising an enzyme or fragment thereof, which enzyme or fragment thereof is able to bind a ligand and is at least 100 amino acids,

wherein said filamentous bacteriophage particles display a population of specific binding pair members, and

separating particles displaying specific binding pair members which bind to said desired ligand.

79. A method according to claim 78 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

28111/32106B

**CLAIMS PENDING AFTER ENTRY OF
AMENDMENT DATED JANUARY 21, 2000**

80. (Amended) A method of obtaining a member of a specific binding pair, the method comprising:
contacting a library of filamentous bacteriophage particles with a desired ligand,
wherein said filamentous bacteriophage particles display on their surface as a fusion with a coat protein surface component a polypeptide which is a specific binding pair member with ability to bind a complementary ligand, the particles containing nucleic acid encoding said fusion, said nucleic acid including a sequence encoding said polypeptide provided by mutation of nucleic acid encoding a specific binding pair member comprising an enzyme or fragment thereof, which enzyme or fragment thereof is able to bind a ligand and is at least 100 amino acids,
wherein said filamentous bacteriophage particles display a population of specific binding pair members, and
separating particles displaying specific binding pair members which have a desired enzymatic activity.

81. A method according to claim 80 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

82. (Amended) A method of obtaining a member of a specific binding pair, the method comprising:
contacting a library of filamentous bacteriophage particles with a desired ligand,
wherein said filamentous bacteriophage particles display on their surface as a fusion with a coat protein surface component a polypeptide which is a specific binding pair member with ability to bind a complementary ligand, the particles containing nucleic acid encoding said fusion, said nucleic acid including a sequence encoding said polypeptide provided by mutation of nucleic acid encoding a specific binding pair member comprising an enzyme or fragment thereof, which enzyme or fragment thereof is able to bind a ligand and is at least 200 amino acids,
wherein said filamentous bacteriophage particles display a population of specific binding pair members, and
separating particles displaying specific binding pair members which bind to said desired ligand.

83. A method according to claim 82 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

28111/32106B

**CLAIMS PENDING AFTER ENTRY OF
AMENDMENT DATED JANUARY 21, 2000**

84. (Amended) A method of obtaining a member of a specific binding pair, the method comprising:

contacting a library of filamentous bacteriophage particles with a desired ligand,

wherein said filamentous bacteriophage particles display on their surface as a fusion with a coat protein surface component a polypeptide which is a specific binding pair member with ability to bind a complementary ligand, the particles containing nucleic acid encoding said fusion, said nucleic acid including a sequence encoding said polypeptide provided by mutation of nucleic acid encoding a specific binding pair member comprising an enzyme or fragment thereof, which enzyme or fragment thereof is able to bind a ligand and is at least 200 amino acids,

wherein said filamentous bacteriophage particles display a population of specific binding pair members, and

separating particles displaying specific binding pair members which have a desired enzymatic activity.

85. A method according to claim 84 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

86. A method of producing a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 78; and

(ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

87. A method according to claim 86 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

88. A method of producing a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 80; and

(ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

89. A method according to claim 88 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

28111/32106B

**CLAIMS PENDING AFTER ENTRY OF
AMENDMENT DATED JANUARY 21, 2000**

90. A method of producing a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 82; and
- (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

91. A method according to claim 90 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

92. A method of producing a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 84; and
- (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

93. A method according to claim 92 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

94. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 78; and
- (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

95. A method according to claim 94 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

96. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 80; and
- (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

97. A method according to claim 96 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

28111/32106B

**CLAIMS PENDING AFTER ENTRY OF
AMENDMENT DATED JANUARY 21, 2000**

98. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 82; and
- (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

99. A method according to claim 98 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

100. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 84; and
- (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

101. A method according to claim 100 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

102. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 78, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and
- (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

103. A method of producing a specific binding pair member, the method comprising:

- producing by expression from encoding nucleic acid obtained by a method according to claim 102 a said derivative specific binding pair member.

28111/32106B

**CLAIMS PENDING AFTER ENTRY OF
AMENDMENT DATED JANUARY 21, 2000**

104. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 80, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

105. A method of producing a specific binding pair member, the method comprising:

producing by expression from encoding nucleic acid obtained by a method according to claim 104 a said derivative specific binding pair member.

106. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 82, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

107. A method of producing a specific binding pair member, the method comprising:

producing by expression from encoding nucleic acid obtained by a method according to claim 106 a said derivative specific binding pair member.

28111/32106B

**CLAIMS PENDING AFTER ENTRY OF
AMENDMENT DATED JANUARY 21, 2000**

108. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 84, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

109. A method of producing a specific binding pair member, the method comprising:

producing by expression from encoding nucleic acid obtained by a method according to claim 108 a said derivative specific binding pair member.